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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/380,835 01/31/00 REY

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LORUSSO & LOUD
440 COMMERCIAL STREET
BOSTON MA 02109

HM22/1106

EXAMINER

HUANG, E

ART UNIT

PAPER NUMBER

1625

DATE MAILED:

11/06/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/380,835

Applicant(s)

Rey

Examiner

Evelyn Huang

Group Art Unit

1625

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-15 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-15 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 3

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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1. Claims 1-15 are pending.

Specification

2. The spacing of the lines of the specification is such as to make reading and entry of amendments difficult. New application papers with lines double spaced on good quality paper are required.

All the chemical structural formulae are missing in the specification.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- a. The structural formulae are missing in the claims.
- b. Claim 1,
 - last line in the definition of R1, what does applicant mean by '*such a hetero-aromatic*'?
 - definition of R2, what is an '*isocyclic system*'? A definition is not found in the specification.
 - a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and

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bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "preferably" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim recites the broad recitation isocyclic system, and the claim also recites which is derived from camphor sulfonic acid, which is the narrower statement of the range/limitation.

---for the reducing agent and the solvent, the proper Markush format is 'the reducing agent chosen from a group consisting of A, B, C *and* D' or 'the reducing agent *is* A, B, C *or* D'.

- c. Claim 6, what does applicant mean by 'fixed in R-position'?
- d. Claim 7,

----a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "preferably" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt

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as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 7 recites the broad recitation alkyl, and the claim also recites ethyl, which is the narrower statement of the range/limitation.

e. Claim 11, it is unclear as to what is intended for 'and/or calcium'.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for the process for the preparation of the compounds in the examples. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

a. Nature of the invention. The invention is drawn to a process for preparing a 1, 4-disubstituted piperidine compound of formula I by reacting a compound of formula II with a piperidone compound of formula III in the presence of an inert solvent and in the presence of a finely dispersed metal compound, or a low valent stage thereof, of the IV and/or V and or VI subgroup of the periodic table, wherein the finely dispersed metal compound, or a low valent stage thereof is produced in situ by means of a reducing agent.

b. State of the prior art/ level of the skilled in the art. The coupling reaction of a tricyclic ketone and a cyclic ketone in the presence of low valent titanium generated by a reducing

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agent is known (Cid; Jackson, 6093827, see paragraph 11 below; Stampa, 6084100, see paragraph 12 below).

The level of the skilled artisan in the preparation art is high.

c. Predictability/unpredictability of the art. The high degree of unpredictability is well known in the chemical art. A slight modification in the structure of the compound may result in drastic changes in the reaction process.

d. Amount of guidance/working examples. The preparation of 4 example compounds limited to unsubstituted or 8-halo-5, 6 dihydro-benzo-[5,6]-cyclohepta[1,2-b]pyridine-11-ylidene-1-piperidine carboxylic acid ethyl ester are prepared using the corresponding 5, 6 dihydro-benzo-[5,6]-cyclohepta[1,2-b]pyridine-11-one and ethoxy carbonyl-4-piperidone in the presence of titanium tetrachloride generated with powdered zinc or zinc-copper alloy.

Starting materials and the process of making the instantly claimed compounds not described in the specification are not seen but required. Sources are particularly pertinent. Absent sources, the public is offered mere language, rather than enablement. Ex parte Moersch 104 USPQ 122. In re Howarthe 210 USPQ 689.

e. Breadth of the claims. Applicant's assertion that all the structurally diverse compounds can be prepared by the instant process employing any metal compound, or a low valent stage thereof, of the IV and/or V and or VI subgroup of the periodic table in the presence of a reducing agent, does not commensurate with that of the objective enablement, especially in view of the high degree of unpredictability in the art and the working examples limited to using low valent titanium generated by zinc (paragraphs c, d).

f. Quantitation of undue experimentation. Since insufficient teaching and guidance have been provided (paragraphs c-e above), one of ordinary skill in the art, even with high degree of skill, would not be able to employ the process for the preparation of all the compounds as claimed without undue experimentation except for using low valent titanium generated by zinc in

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the coupling reaction for the preparation of unsubstituted or 8-halo-5, 6 dihydro-benzo-[5,6]-cyclohepta[1,2-b]pyridine-11-ylidene-1-piperidine carboxylic acid or its ester.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Piwinski I (WO 89/10369, PTO-1449). The compounds described on pages 54- 55 (compounds E, F, G), pages 64-66 (compounds E, F,G) are encompassed by the instant claim.

7. Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Piwinski II (5089496, PTO-1449). The compounds described on columns 71-74 (Table IV) are encompassed by the instant claim.

8. Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Wong I (EP 515158, PTO-1449). The compounds described on pages 22-23 (compounds F, G and Example 1) are encompassed by the instant claim.

9. Claim 15 is rejected under 35 U.S.C. 102(b) as being anticipated by Wong II (EP 524784, PTO-1449). The 3 compounds described on page 21 are encompassed by the instant claim.

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10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

11. Claims 1-13, 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Jackson (6093827). The process of Example 3 (column 5) and the compound, loratidine, are encompassed by the instant claims.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

12. Claims 1-13, 15 are rejected under 35 U.S.C. 102(e) as being anticipated by Stampa (6084100). The process of Example 1 (column 5) and the compound, loratidine, (claims 1-13) are encompassed by the instant claims.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jackson (6093827).

Jackson generically discloses a process for preparing a 10, 11, -dihydro-5H-dibenzo [a,d]-cyclohept-11-ene or an azo derivative thereof by reacting a dibenzosuberone or an aza derivative thereof with a cyclic aliphatic ketone in the presence of low valent titanium which is generated by zinc (columns 5-6, claims 1-1, 13; columns 7-8, claims 14-17). A specific example is described on column 5, Example 3.

The compound of Example 3 differs from the instant compound of Example 14 in having a 8- chloro instead of the instant 8-fluoro substituent.

Jackson, however, teaches that chloro or fluoro are optional choices for R2 (column 5, lines 55-6).

At the time of the invention, the skilled artisan would be motivated to prepare the alternative 8-fluoro-substituted compound using the process described by Jackson to arrive at the instant invention since Jackson had clearly taught that the process is effective for the preparation of any compounds within the disclosed genus.

Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

15. Claims 1-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Piwinski II (5089496, PTO-1449) in view of Cid.

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Piwinski generically discloses the instant compound (columns 1-3) and its process of making (column 26). Specific compounds are described in Table IV. A process is specifically described on column 50.

Piwinski's process involves the reaction of a 5,6-dihydro-1H-benzo[5,6]cyclohepta[1,2-b]pyridine-11-one with a Grignard reagent prepared from N-methyl-4-chloro-piperidine to form the piperidynyl-5,6-dihydro-1H-benzo[5,6]cyclohepta[1,2-b]pyridine-11-ol followed by conversion to the corresponding piperidylene. The instant is an alternative process wherein Piwinski's 5,6-dihydro-1H-benzo[5,6]cyclohepta[1,2-b]pyridine-11-one is reacted with a piperidone in the presence of an inert solvent and a low valent titanium produced by a reducing agent in situ.

The direct mixed carbonyl coupling reaction of the instant is described by Cid (page 6197, scheme 1).

At the time of the invention, to achieve a more efficient and simple synthesis of the piperidylene compound, one of ordinary skill in the art would be motivated to modify Piwinski's process by directly coupling the 5,6-dihydro-1H-benzo[5,6]cyclohepta[1,2-b]pyridine-11-one with the piperidone as taught by Cid to arrive at the instant invention.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is (703) 305-7247.

October 26, 2000



EVELYN MEI HUANG
PRIMARY EXAMINER